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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/817,483	04/02/2004	Jeffrey E. Habben	0803R	3903

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EXAMINER	
BAUM, STUART F	
ART UNIT	PAPER NUMBER
1638	

NOTIFICATION DATE	DELIVERY MODE
08/05/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/817,483	HABBEN ET AL.	
	Examiner	Art Unit	
	STUART F. BAUM	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,19,33-37,44,50-54,68 and 69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,19,33-37,44,50-54,68 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/13/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 5/13/2008 has been entered.

RCE Acknowledgment

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/13/2008 has been entered.

3. Claims 18-19, 33-37, 44, 50-54 and 68-69 are pending.

Claims 20-32, 38-43, 45-49 and 55-67 have been canceled.

4. Claims 18-19, 33-37, 44, 50-54 and 68-69, including SEQ ID NO:1, 3 and 4 are examined in the present office action.

5. Rejections and objections not set forth below are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 18-19, 33-37, 44, 50-54 and 68-69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is indefinite in the recitation "zag2.1, ZAP, tb1, PCNA2 and kn1". The sole designation of nucleotide sequences by "zag2.1, ZAP, tb1, PCNA2 and kn1" is arbitrary and

creates ambiguity in the claims. For example, the nucleotide sequences in this application could be designated by some other arbitrary means, or the assignment of said name could be arbitrarily changed to designate a different nucleotide sequence. If either event occurs, one's ability to determine the metes and bounds of the claim would be impaired. See *In re Hammack*, 427 F .2d 1378, 1382; 166 USPQ 204, 208 (CCPA 1970). Amendment of the claim to recite maize zag2.1, maize ZAP, maize tb1, maize PCNA2 will obviate the rejection as it applies to the recitation "zag2.1, ZAP, tb1 and PCNA2". All subsequent recitations of zag2.1, ZAP, tb1, PCNA2 or kn1 are also rejected.

Claim 18 is indefinite for reciting "enhanced vigor". Applicants have not disclosed the metes and bounds of "enhanced vigor". It is not clear what parameters would be measured to determine if a plant is exhibiting "enhanced vigor". All subsequent recitations of "enhanced vigor" are also rejected.

Written Description

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 18-19, 33-37, 44, 50-54 and 68-69 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a transgenic plant and method comprising in part a promoter selected from the group consisting of zag2.1, ZAP, tb1, PCNA2 and kn1.

Applicants disclose the maize gene ZAG2 was isolated based on homology to the Arabidopsis AGAMOUS gene, which directs floral development (page 32, 1st full paragraph). Applicants disclose ZAG2 is normally expressed in developing female florets. The protein coding sequence and 2.1 kb of 5' sequence is deposited in GenBank accession no. X80206. Applicants disclose a portion of the ZAG2 5' sequence is designated as ZAG2.1 promoter whose sequence is set forth in SEQ ID NO:3 (*Ibid*). Applicants disclose the ZAP promoter sequence is disclosed in SEQ ID NO:5, the tb1 promoter sequence is disclosed in SEQ ID NO:17 and the PCNA2 sequence is disclosed in SEQ ID NO:25 (page 16). Applicants disclose SEQ ID NO:3, 5, 17 and 25 are from maize (for ZAG2.1 see above, for ZAP see page 16, for tb1 see page 31, lines 23-24, for PCNA see page 31, line 29).

The Office contends, the claims as written encompass 5 genera of different promoter sequences, i.e., the genus of zag2.1 promoters, the genus of ZAP promoters and so on.

Applicants have not disclosed essential regions for each of the five promoter sequences that are identified as zag2.1, ZAP, tb1, PCNA2 and kn1, nor have Applicants disclosed a representative number of promoter sequences for each of the five promoter genera.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court

stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences having zag2.1, ZAP, tb1, PCNA2 and kn1 promoter activity. Applicants only describe the maize ZAG2.1 promoter whose sequence is set forth in SEQ ID NO:3, or the maize ZAP promoter whose sequence is disclosed in SEQ ID NO:5, or the maize tb1 promoter whose sequence is disclosed in SEQ ID NO:17, or the maize PCNA2 promoter whose sequence is disclosed in SEQ ID NO:25. Furthermore, Applicants fail to describe structural features common to members of the claimed genera of promoter sequences. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the different promoter sequences, it remains unclear what features identify a maize zag2.1, ZAP, tb1 and PCNA2 promoter. Since the genera of promoters have not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims. Amending the claims to recite maize zag2.1,

maize ZAP, maize tb1 and maize PCNA2, will obviate the rejection as it applies to the recitation "zag2.1, ZAP, tb1 and PCNA2".

Enablement

8. Claims 18-19, 33-37, 44, 50-54 and 68-69 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to a transgenic plant or method of modulating cytokinin activity in a plant comprising transforming a plant with a recombinant expression cassette comprising a promoter selected from the group consisting of zag2.1, ZAP, tb1, PCNA2 and kn1 operably linked to a polynucleotide encoding isopentenyl transferase isolated from Agrobacterium, Arabidopsis or Petunia, wherein said transgenic plant displays enhanced vigor compared to a

corresponding plant without said cassette, or wherein the cassette comprises SEQ ID NO:3 operably linked to the coding region of SEQ ID NO:1 and SEQ ID NO:4.

Applicants disclose data for one construct comprising the zag2.1 promoter operably linked to a nucleic acid encoding ipt and transformed into maize (page 107, lines 3-4). Applicants state: "Results are shown in Figure 3. Grain yield of seven of the nine events was greater than that of controls. Kernel number, ear length, and kernel mass were also measured; results for transgenics exceeded those for non-transgenic sibs in five out of nine events for ear length; and in five out of nine events for both kernel number and dry matter per kernel (page 108, 2nd paragraph). Applicants state "Five of the nine events showed a statistically significant increase in plant height, as shown in Figure 4" (page 108, 4th paragraph). Applicants state "As shown in Figure 5, three of the nine events showed a statistically significant increase in yield, including two of the events also showing increased plant height. Ear number, kernel number, and kernel mass were also measured, as shown in Figure 6" (paragraph bridging pages 108-109). Applicants state "Five of the nine events showed a statistically significant increase in plant height, as shown in Figure 7. Four of these five, and one additional event, showed increased leaf greenness, as shown in Figure 8" (page 109, 2nd full paragraph). Applicants state "Three of the nine events gave improved yield results, as shown in Figure 9; all three of these events had also displayed increased plant height and leaf greenness. The increase in plant biomass for one of these events is shown in Figure 10" (page 109, 3rd full paragraph).

The Office contends the above construct, i.e., zag2.1::ipt is included in the enablement rejection in part because it is not clear how the data in the graphs was calculated (see for example Figures 2-9). Applicants are invited to further explain how the data in the graphs was calculated,

i.e., why for example does "Event 15846" in Figure 2 have a negative "Ear Growth Rate". In addition, the claims recite enhanced vigor, but as stated above in the 112 2nd rejection, it is not clear to what enhanced vigor applies. Applicants have not stated a nexus between enhanced vigor and the phenotypic characteristics disclosed above.

Re: the ZAP, tb1, PCNA2 and kn1 promoters have not been exemplified by Applicant, nor has Applicant disclosed the spatial and temporal expression patterns of these promoters and how they relate to zag2.1. Applicants have not disclosed why these promoters can work in place of the maize zag2.1 promoter. For example, Jackson et al (1994, Development 120:405-413) discloses the maize KNOTTED1 gene is expressed in the shoot meristems, including the vegetative, inflorescence and floral meristems and developing stems but not in determinate lateral organs (abstract). The state-of-the-art teaches expressing IPT in a plant produces unexpected results. Sa et al (2002, Transgenic Research 11(3):269-278) report that transformed tobacco with IPT from Agrobacterium under the control of a promoter which specifically expresses in anthers, resulted in perturbation in the development of anthers and pollen (abstract). Therefore, without empirically testing each promoter::IPT construct, one of skill in the art cannot predict which promoters will produce a plant with the expected phenotype.

The IPT genes from Arabidopsis and Petunia exhibit low levels of similarity with IPT from Agrobacterium and do not produce the same forms of cytokinin. Takei et al (2001, The Journal of Biological Chemistry276(28):26405-26410; listed in IDS) disclose eight IPT genes from Arabidopsis exhibited 37%, 33%, 41%, 45%, 41%, 41%, 42%, and 44% amino acid similarity when compared to the Agrobacterium IPT gene, tmr (page 26406, right column, 4th paragraph). Takei et al also suggests that further experimentation is required to elucidate the

physiological function of the different IPT genes in Arabidopsis (page 26409, right column, 3rd full paragraph). Zubko et al (The Plant Journal 29(6):797-808; listed in IDS) disclose that the Petunia homolog of the bacterial IPT gene (named SHO) produces different products compared to IPT. Sho produces 2iP9G and 2iP7G in Petunia while IPT mainly produces zeatin and zeatin ribosides (page 803, right column, top paragraph). Therefore, given the different end products of the IPT gene from Agrobacterium and the SHO gene from Petunia, it is not clear if one skilled in the art can expect the same phenotype using the SHO gene as is generated using the bacterial IPT gene.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified constructs by either by using non-disclosed fragments of the Zag2.1 promoter of SEQ ID NO:3, or fragments of the ZAP promoter of SEQ ID NO:5, or fragments of the tb1 promoter of SEQ ID NO:17, or fragments of the PCNA2 promoter of SEQ ID NO:25, or non-disclosed regions of any kn1 promoter as probes or by designing primers to undisclosed regions of the Zag2.1 promoter of SEQ ID NO:3, or the ZAP promoter of SEQ ID NO:5, or the tb1 promoter of SEQ ID NO:17, or the PCNA2 promoter of SEQ ID NO:25, or non-disclosed regions of any kn1 promoter and isolating or amplifying fragments, subcloning the fragments, producing expression vectors comprising the isolated or amplified promoter fragment operably linked to a nucleic acid encoding the Agrobacterium, Arabidopsis or Petunia isopentenyl transferase and transforming plants therewith, in order to identify those, if any, that exhibit an enhanced vigor, whose meaning is not defined.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

9. Claims 18-19, 33-37, 44, 50-54 and 68-69 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest a transgenic plant or a method of modulating cytokinin activity in a plant comprising transforming a plant with a recombinant expression cassette comprising a promoter of zag.1, ZAP, tb1, PCNA2 or kn1 operably linked to a polynucleotide encoding isopentenyl transferase isolated from Agrobacterium, Arabidopsis or Petunia.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached at 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

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/Stuart F. Baum/
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Art Unit 1638
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